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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,780	02/20/2004	Asa Abeliovich	5199-70	6675

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
06/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/783,780	ABELIOVICH ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 24-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 02/28/07 has been acknowledged.

Claims 20-23 are examined in this office action.

This application contains claims 1-19 and 24-67 drawn to an invention nonelected with traverse in the reply filed on 06/02/06. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

Claim Rejections - 35 USC § 112

Claims 21-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reason of record as set forth in the office action mailed on 08/29/06.

Nature Of Invention

The invention of instant claim relates to a method for treating a neurodegenerative diseases via method for gene therapy.

Breadth Of Claims And Guidance Provided in the Specification

The scope of invention as claimed encompasses the treatment of any neurodegenerative diseases especially sporadic Parkinson's disease or autosomal recessive early-onset Parkinson's disease by administering a lentiviral vector encoding human parkin protein, wherein the lentiviral vector is administered to the subject via any and all routes of administration.

Response to Argument (enablement)

The applicant argues that the specification teaches that a therapeutic agent like resveratrol shown to protect neuronal cells in an in-vitro kainic acid model system using neuronal cells, is also capable of protecting neuronal cells in-vivo in kainic acid animal models of neurodegeneration. These studies show that, in the kainic acid model of neurodegeneration, a therapeutic effect demonstrated in vitro can be translated to an in-vivo therapeutic effect. Based upon these arguments the applicant concluded that in-vitro kainic acid model of neurodegeneration demonstrating a therapeutic effect of a therapeutic composition, comprising (a) a lentiviral vector comprising a nucleic acid encoding a human parkin protein; and (b) a pharmaceutically-acceptable carrier supports claims directed to methods for treating neurodegeneration in a subject comprising administering to the subject the claimed therapeutic composition in an amount effective to treat the neurodegeneration in the subject. The applicant argues that one of skill in the art would understand how to admlmster a lentivtral vector encoding a parkin protein to a subject. The art at the time of filing provides guidance for introducing a therapeutic gene therapy lentiviral vector into, for example, a mammalian brain, including a nonhuman primate brain. Regarding multifactorial etiology of Parkinson's disease and unpredictability involved in the treatment of the Parkinson's disease the applicant argues that it is not necessary to know the underlying molecular determinants of a disorder in order to develop a method for treating the disorder.

However the applicant's arguments are found not persuasive. Applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

The applicant fails to consided that invention as claimed encompasses is drawn to a method for treatment of any neurodegenerative diseases especially sporadic Parkinson's disease or autosomal recessive early-onset Parkinson's disease by administering a lentiviral vector encoding human parkin protein, wherein the lentiviral vector is administered to the subject via any and all routes of administration. Therefore the invention as claimed falls in the realm of gene therapy, which is considered highly unpredictable in contrast of any protein of drug therapy.

Furthermore, It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (*See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970).

The earlier office action provides clear evidence that the gene therapy is considered highly experimental area of research at this time, and both researchers and the public agree that demonstrable progress to date has fallen short of initial expectations. Furthermore, Recombinant DNA Advisory committee (RAC) also emphasized that expectations of current gene therapy protocols have been over sold without any apparent success. The advisory panel further emphasized the need for a greater understanding of an underlying mechanism that contribute to a genetic disease along with the pathogenesis of the disease.

In instant case the scope of invention as claimed encompasses the treatment of any neurodegenerative diseases especially sporadic Parkinson's disease or autosomal recessive early-onset Parkinson's disease by administering a lentiviral vector encoding human parkin protein, wherein the vector is administered to the subject via any and all routes of administration. The specification as filed fails to disclose that the administration of a lentiviral vector encoding human parkin protein result in the treatment of any neurodegenerative diseases as broadly claimed herein. The specification even fails to provide an enabling disclosure that would enable one skilled in the art to treat sporadic Parkinson's disease or autosomal recessive early-onset Parkinson's disease by administering a lentiviral vector encoding the parkin protein. *At best the specification provides in-vitro transformation of isolated neuronal cells, which does not recapitulate the complex ties involved in a method associated with gene therapy.*

Furthermore, the earlier office action provides clear evidence that the etiology of Parkinson's disease (PD) is multifactorial and complex (see Abliovivh et al J. Neurochem10.111/j.1471-459, 2006.04102.x, which renders the treatment of PD (especially via gene therapy) highly unpredictable. For example, the current animal and tissue culture systems are able to mimic some of the pathology and morphology of idiopathic PD. However, identifying the molecular determinants involved in PD without any a priori knowledge of the mechanism of the neurodegeneration is significantly hindered due to the lack of a definitive model system. In addition, if PD in humans is a multifactorial disease, controlled delivery and expression of a gene even by using an inducible and a safe vector, may only provide partial benefit for the patient. Because typical PD is likely to be determined by environmental factors, and age is a consistent risk factor, it is necessary to understand first what factors are responsible in an age dependent manner for the selective loss of nigrostriatal neurons before an efficient strategy for its prevention can be undertaken (see Nass et al, Parkinsonism Relat Disord. (3):185-191. 2001; Shastry Neuroscience Research 41:5-12, 2001).

Regarding the route of administration of the gene tic vector the applicant fails to consider that the transduction of target cells represents the first critical step in gene

therapy, which not only depends upon the type of target cells but also on the choice and/or characteristics of delivery vectors. In addition, besides the limitations in gene transfer the problem to selectively target cells in vivo is still one of the most difficult obstacles to overcome. The viral particles binds to many cells they encounter in vivo and therefor would be diluted out before reaching their targets. In the instant case the scope of invention as claimed encompasses the administration of a genetic construct (as claimed) via any and all routes of administration (i.e. oral, nasal systemic, intramuscular, intradermal etc). Although, the gene therapy holds much promise to come, the success will only be achieved through continued rigorous research on the most fundamental mechanisms that contribute to a genetic disease along with the pathogenesis of the disease, gene delivery and gene expression in animals.

In instant case treatment of any neurodegenerative disease especially sporadic Parkinson's disease or autosomal recessive early-onset Parkinson's disease by administering a lentiviral vector encoding human parkin-protein is not considered routine in the art and without sufficient evidence the demonstrates the treatment of neurodegenerative disease (as claimed) via administration of a lentiviral vector encoding the human parkin-protein to a specific location the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore considering the state of the art and limited amount of guidance provided in the instant specification, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Claim 23 (as amended) provides for the use of a therapeutic composition of claim 20, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite

where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 23 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). In the instant case (claim 23), it is unclear for what the composition as claimed is used especially in context of an animal model of Parkinson's disease.

Claim Rejections - 35 USC § 102

Claim 20 is rejected under 35 U.S.C. 102(e) as being anticipated by Kingsman (US 2003/0180740 A1 2003), for the reason of record as set forth in the office action mailed on 08/29/06.

Response to Argument (35 USC102)

The applicant argues that Kingsman does not disclose in an enabling manner production of a therapeutic composition, comprising (a) a lentiviral vector comprising a nucleic acid encoding a human parkin protein; and (b) a pharmaceutically-acceptable cartier. The applicant argues that Kingsman does not disclose particular materials and a particular methodology to produce the subject matter of the claim. There are no methods disclosed in Kingsman which are particular to parkin, nor is there any disclosure of materials which are particular to parkin.

However the applicant's arguments are found not persuasive. The cited art clearly teaches a lentiviral vector encoding the parkin protein (see page 42-43). Standard for what constitutes sufficient enablement of prior art reference for purposes of anticipation under 35 U.S.C. §102 differs from enablement standard under Section 112, in that prior art reference need not demonstrate utility in order to serve as anticipating reference under Section 102; in present case, finding that prior European patent

application failed to adequately disclose utility for claimed method of treating prostate cancer by using finasteride to inhibit production of enzyme 5-α-reductase is insufficient to support conclusion that European application is not enabling reference for purposes of anticipation. Rasmusson v. SmithKline Beecham Corp., 75 USPQ2d 1297 (Fed. Cir. 2005). In the instant case all that is required is a lentiviral vector encoding parkin protein, which is clearly disclosed in the cited art of record. Thus the cited art clearly anticipate the invention as claimed.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SUMESH KAUSHAL
PRIMARY EXAMINER